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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,371	02/15/2002	Kalyan Handique	10255-029-999	9738
26171	7590	09/13/2006		
FISH & RICHARDSON P.C. P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022				
			EXAMINER SINES, BRIAN J	
			ART UNIT 1743	PAPER NUMBER

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/075,371

**Applicant(s)**

HANDIQUE ET AL.

**Examiner**

Brian J. Sines

**Art Unit**

1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 6/23/2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 32-78 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 32-78 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION*****Drawings***

The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, with respect to claim 44, the laboratory robot must be shown or the feature(s) canceled from the claim(s). In figure 1, it is unclear as to how the sample input and the reagent input module is structurally configured to accept material from laboratory robot 154. In addition, the laboratory robot 154 is not shown in figure 3 as indicated by the specification on pages 6 and 7. No new matter should be entered.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50 – 56 and 74 – 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 50 – 56 and 74 – 78 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are:

Regarding claim 50, it is unclear as to how the flow-through member and enrichment chamber are fluidically connected. Regarding claim 74, it is unclear as to how the vent, first valve and second valve are fluidically connected. The claims merely recite a listing of features with no indication of how the features are connected in order to operate. The structure which goes to make up the device must be clearly and positively specified. The structure must be organized and correlated in such a manner as to present a complete operative device.

Claim 74 recites the limitation "mixing zone" in line 4. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

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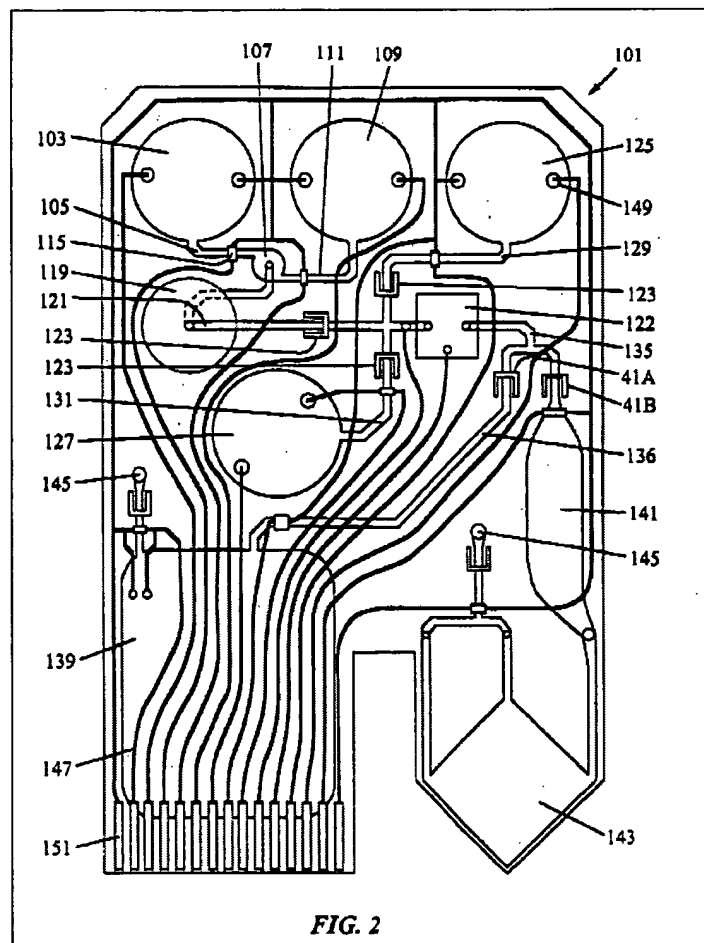
such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 32 – 61 and 63 – 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pourahmadi et al. (U.S. Pat. No. 6,664,104 B2) (hereinafter “Pourahmadi”) in view of Handique et al. (U.S. Pat. No. 6,130,098 A) (hereinafter “Handique”).

Regarding claims 32, 49, 50, 53, 57 – 61, 63, 64, 66, 68, 69, 70, 72 – 74 and 76, Pourahmadi teaches a microfluidic device 101 comprising: an enrichment module or zone (flow-through component 122); a cell lysing module 119; a mixing module 107; and a DNA manipulation module 143 for performing PCR amplification (see col. 4, line 65 – col. 6, line 47; figure 2). Pourahmadi teaches the incorporation of valves for facilitating fluid flow control within the disclosed device (see, e.g., col. 14, lines 39 – 51).

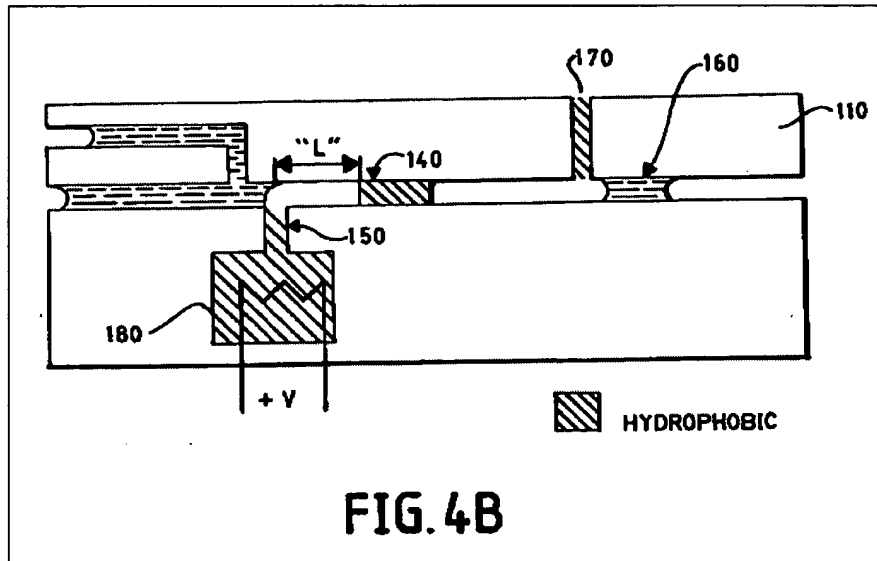


Pourahmadi does not specifically teach the incorporation of a microdroplet preparation module. Pourahmadi does teach that a fluid sample may be introduced into the cartridge by a variety of means, manual or automated (see col. 10, lines 32 – 40). In particular, Pourahmadi does teach that a pneumatic fluid motive source may be incorporated within the device (see, e.g., col. 8, lines 27 – 42).

Handique teaches a system and methods for microdroplet preparation with microfluidic devices. Handique further teaches a thermopneumatic apparatus for facilitating fluid transport in microfluidic devices (see col. 13, line 60 – col. 15, line 40; figures 3A, 3B, 4A & 4B). As shown in figure 4B, the system taught by Handique comprises a thermopneumatic gas actuating system

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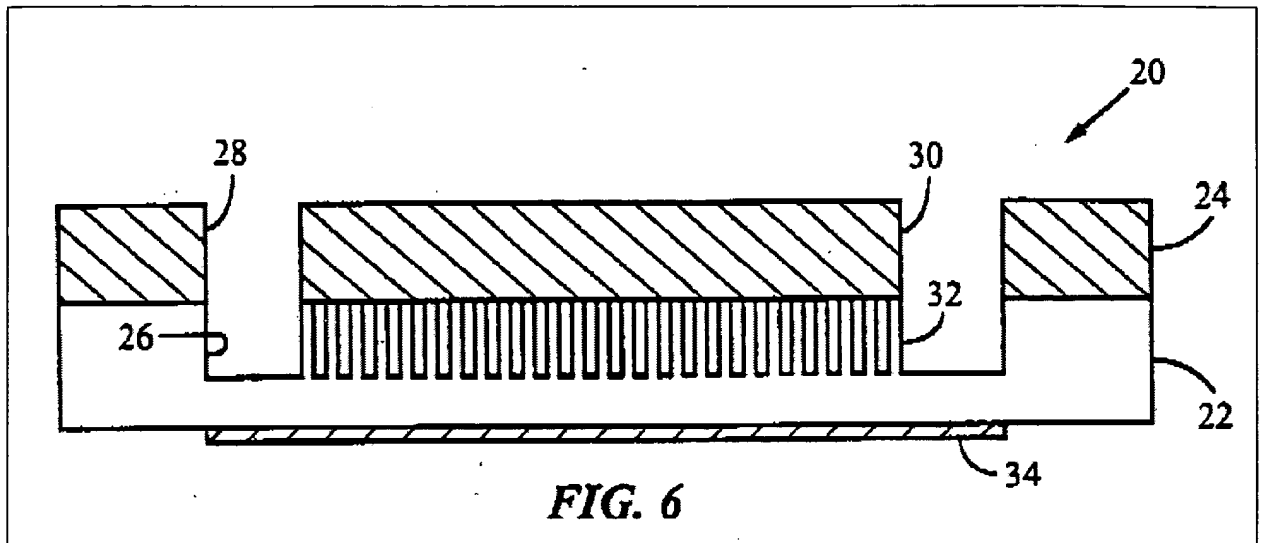
denoted by 180, a hydrophobic gas vent 170, and an outlet, which is located to the right of the sample 160 and at the end of the channel containing the sample. Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate a microdroplet preparation module with an associated actuator as claimed to facilitate sample fluid transport. Handique further teaches that the disclosed microdroplet preparation module comprising a non-wetting positioning element (e.g., a hydrophobic patterned surface) can be configured to split microdroplet samples (see, e.g., col. 30, lines 44 – 57).



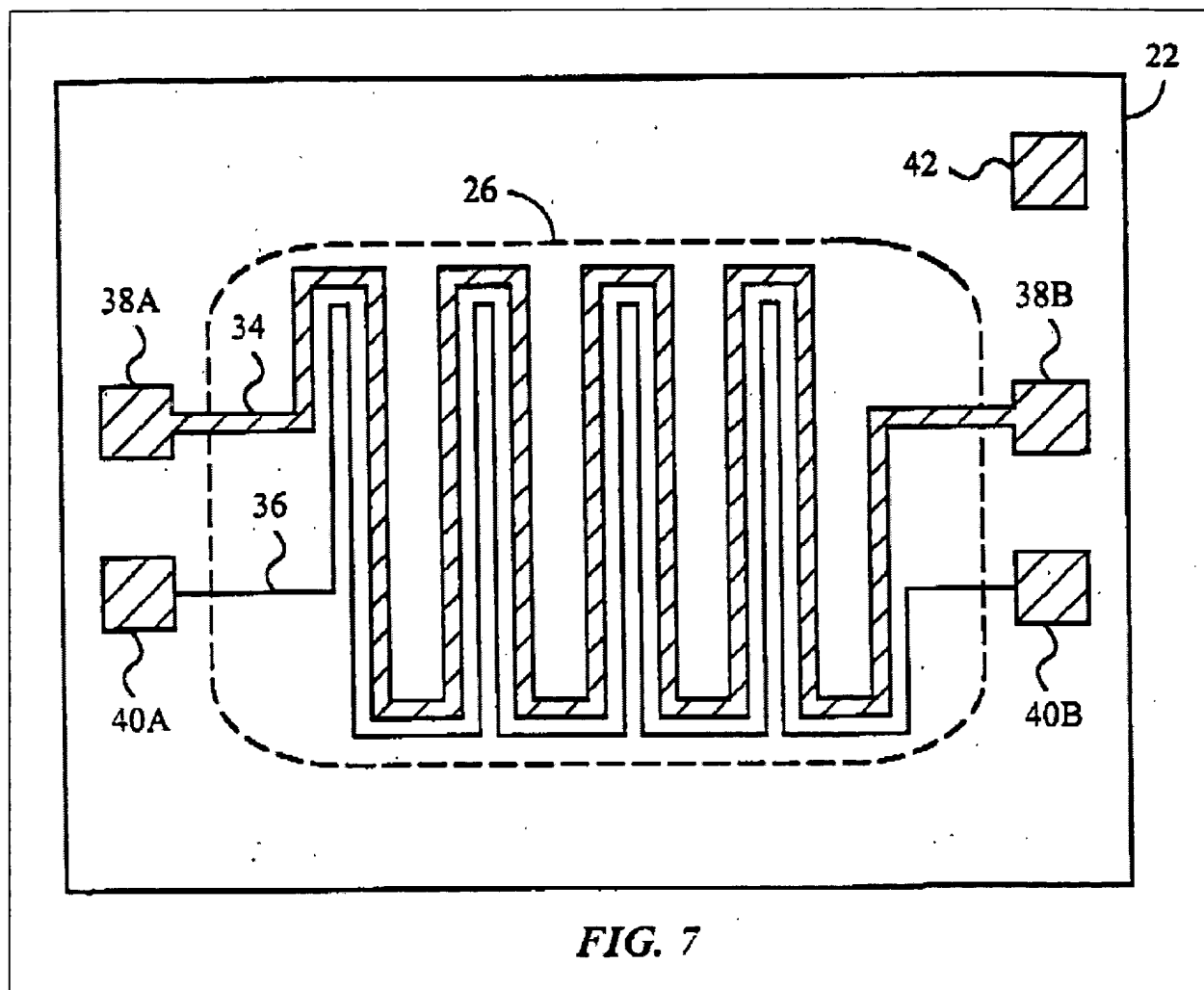
Regarding claims 33 – 36, Pourahmadi teaches that the disclosed device comprising a base substrate 22 and a top substrate 24 having a chamber 26 may be microfabricated using glass or silicon dioxide (see, e.g., col. 13, lines 38 – 67; col. 22, lines 6 – 58; col. 27, lines 6 – 12; figures 6 and 7). The selection of a known material, which is based upon its suitability for the intended use, is within the ambit of one of ordinary skill in the art (see MPEP §2144.07). Pourahmadi further teaches the incorporation of single resistive heating element 34 on the base substrate 22 (see, e.g., col. 31, lines 24 – 48).

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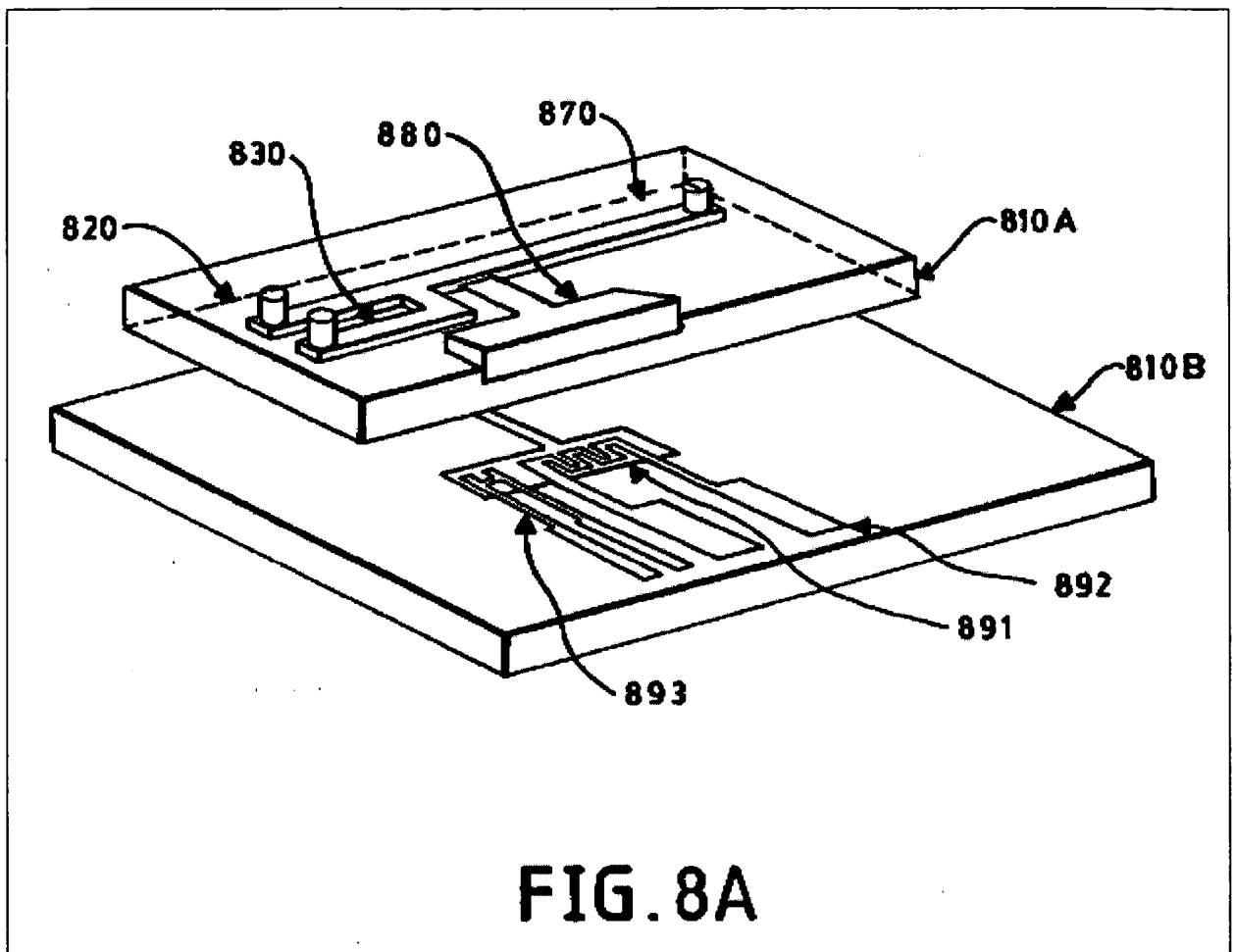
Pourahmadi does not specifically teach the complete device configuration as claimed.



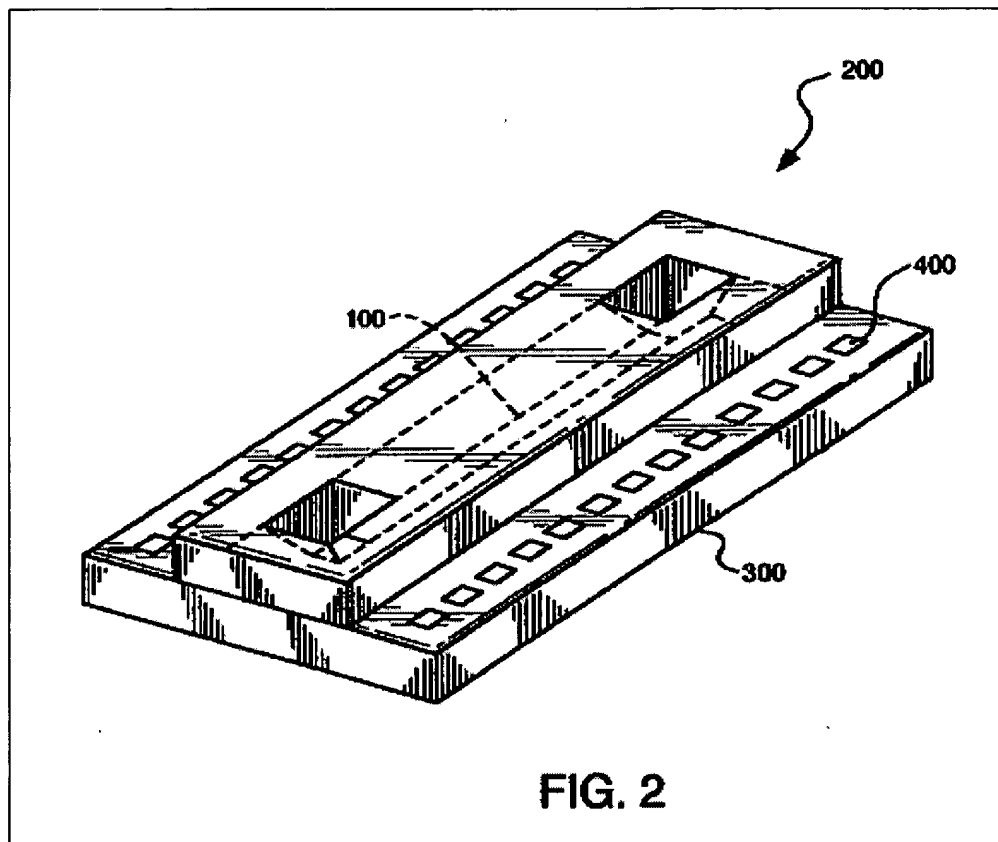




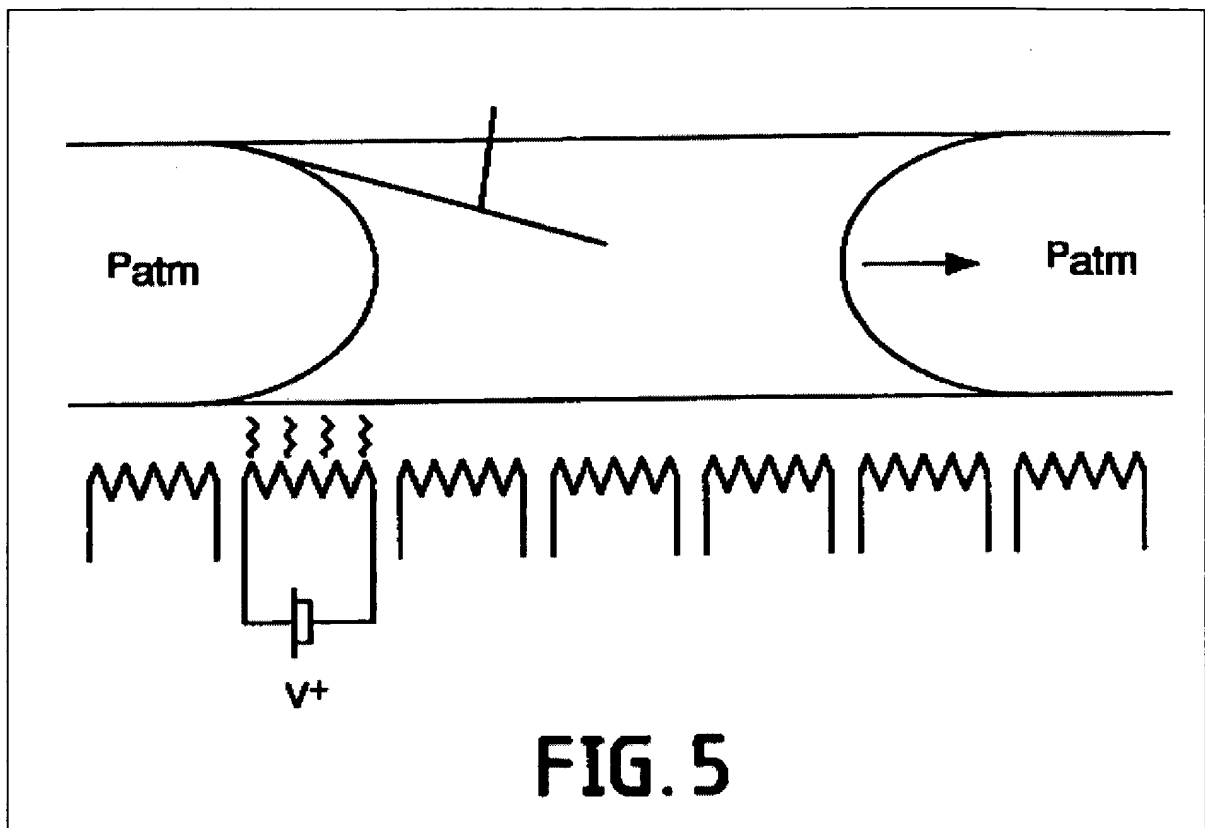
Handique teaches a microfluidic device configuration comprising a lower silicon dioxide substrate 810B and an upper glass substrate 810A. The bottom surface of the upper glass substrate 810A has channels and chambers etch into it. The lower silicon substrate comprises a heating element 891 (see col. 20, lines 5 – 13; col. 26, lines 1 – 29; figure 8A). The resistive heating elements comprise a metallic aluminum film (see col. 20, lines 13 – 22). The substrate layers are bonded together (see, e.g., col. 21, lines 29 – 33).



Handique further teaches a device configuration comprising a lower substrate 300 having a base comprising glass and an upper substrate 200 comprising silicon. The top substrate 200 has microchannels 100 (see col. 13, lines 48 – 59).



As indicated in figure 5, a plurality of successive heaters can be arranged in a substrate and along the length of a channel for facilitating fluid transport through the channel (see col. 15, line 41 – col. 16, line 23).



Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the device configuration within the disclosed microfluidic device as claimed to facilitate effective fluid sample transport.

Regarding claims 37 – 39, Handique teaches microchannel size dimensions that are typically used in microfluidic devices. For example, Handique teaches microchannels having a depth of 0.5 to 50  $\mu\text{m}$  and a width of 20 to 1,000  $\mu\text{m}$  (see col. 7, lines 53 – 63).

Regarding claim 40, Handique teaches the incorporation of contact pads, electric leads or terminals 892 associated with heater 891 and which is exposed at the edge of the lower substrate 810B (see col. 20, lines 5 – 12; figure 8A). In addition, Handique teaches the incorporation of electrical pads or terminals 400 on the edge of lower substrate 300 in the device shown in figure 2.

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Regarding claims 41 and 42, Pourahmadi teaches the incorporation of processing electronics for controlling the operation of the disclosed cartridge (see col. 7, lines 55 – 67; col. 18, lines 48 – 67; col. 19, lines 1 – 65). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate a digital acquisition and control board, e.g., a computer control device, for controlling the operation of the disclosed device.

Regarding claims 43, 44 and 48, Pourahmadi teaches the incorporation of an input means for facilitating the introduction of reagents and test samples into the device (see col. 11, lines 1 – 53). The use of laboratory robots for facilitating sample transfer and analysis are well known in the analytical chemistry and microfluidic device art. In addition, to provide a mechanical or automatic means to replace manual activity, which accomplishes the same result, is within the ambit of a person of ordinary skill in the art. It would have been obvious to a person of ordinary skill in the art to incorporate the use of an automated robot to facilitate sample transfer and input with the disclosed device.

Regarding claims 44 – 47 and 67, these claims are considered recitations of intended use. These claims provide no further specific structure for the claimed microfluidic device to which the claims are directed. Pourahmadi teaches that the disclosed device is capable of processing cells and performing DNA/RNA analysis (see col. 3, lines 26 – 40; col. 5, lines 36 – 40; col. 6, lines 8 – 33).

Regarding claims 51 and 52, Pourahmadi teaches that the flow-through component 122 can comprise a chamber comprising an absorbent material, such as filters, beads, fibers, membranes, polymers and gels (see, e.g., col. 6, lines 1 – 7; figure 2).

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Regarding claims 54 and 55, Handique teaches the incorporation of a single thermopneumatic gas actuator (e.g., chamber 180 including the resistive heater) located beneath a channel within device 110 (see, e.g., figure 4A; col. 14, line 58 – col. 15, line 21). As shown in figure 5 above, Handique teaches the incorporation of a plurality of successive heating elements located underneath a single channel or chamber within the disclosed device for moving fluid through the device. The mere duplication of parts, without any new or unexpected results, is within the ambit of one of ordinary skill in the art (see MPEP § 2144.04). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate a plurality of resistive heating elements within the disclosed device as claimed in order to facilitate effective fluid transport.

Regarding claim 56, as indicated in figure 8A, Handique teaches that when the device is fully assembled, the heater 891 in the lower substrate 810B is joined with the chamber 880 in the top substrate 810A, thereby forming the thermopneumatic gas actuator located within and spanning both of the substrates. The incorporation and use of a one-piece, integrated construction instead of the structure disclosed or taught in the prior art would have been within the ambit of a person of ordinary skill in the art (see MPEP § 2144.04). Therefore, it would have been obvious to a person of ordinary skill in the art to integrate a gas actuator with the upper substrate of the disclosed device as claimed.

Regarding claim 65, as shown in figure 2, Pourahmadi teaches that mixing module 107 comprises various connecting channels (e.g., channels 111, 105, etc.).

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Regarding claims 74 and 77, Pourahmadi further teaches the incorporation of resistive heat sources with the DNA manipulation zone for controlling PCR amplification (see, e.g., col. 18, lines 48 – 67).

Regarding claim 75, Pourahmadi teaches the incorporation of a detector (e.g., a photodetector) in communication with the DNA manipulation zone for monitoring chemical reactions (e.g., PCR) (see, e.g., col. 17, lines 47 – 67).

Regarding claim 78, Pourahmadi teaches the incorporation of light emitting diodes (LED's) in the DNA manipulation zone that can induce or accelerate chemical reactions (see, e.g., col. 17, line 46, line 46 – col. 18, line 12).

2. Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pourahmadi Handique and further in view of Briscoe et al. (U.S. Pat. No. 6,544,734 B1) (hereinafter “Briscoe”).

Pourahmadi indicates that the use of an electrical current can be used to induce cell lysis and extraction for further processing (see col.16, lines 40 – 48).

Briscoe teaches a similar microfluidic device for DNA analysis incorporating a cell lysis chamber 150 comprising one or more electrodes for facilitating cell lysis (see, e.g., col. 10, line 52 – col. 11, line 12). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate a cell lysing mechanism with the disclosed device as claimed for facilitating effective cell lysis and sample analysis.

### ***Response to Arguments***

Applicant's arguments and amendments with respect to the present claims have been considered but are moot in view of the new ground(s) of rejection.

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*Conclusion*

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additional cited prior art teach related microfluidic devices.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Sines whose telephone number is (571) 272-1263. The examiner can normally be reached on Monday - Friday (11 AM - 8 PM EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

A handwritten signature in black ink, appearing to read "Brian J. Sines". The signature is stylized with a large, looping initial "B" and a long, sweeping underline.